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ARTICLE

Solvent- and anion-dependent rearrangement of fluorinated carbene ligands provides access to fluorinated alkenes

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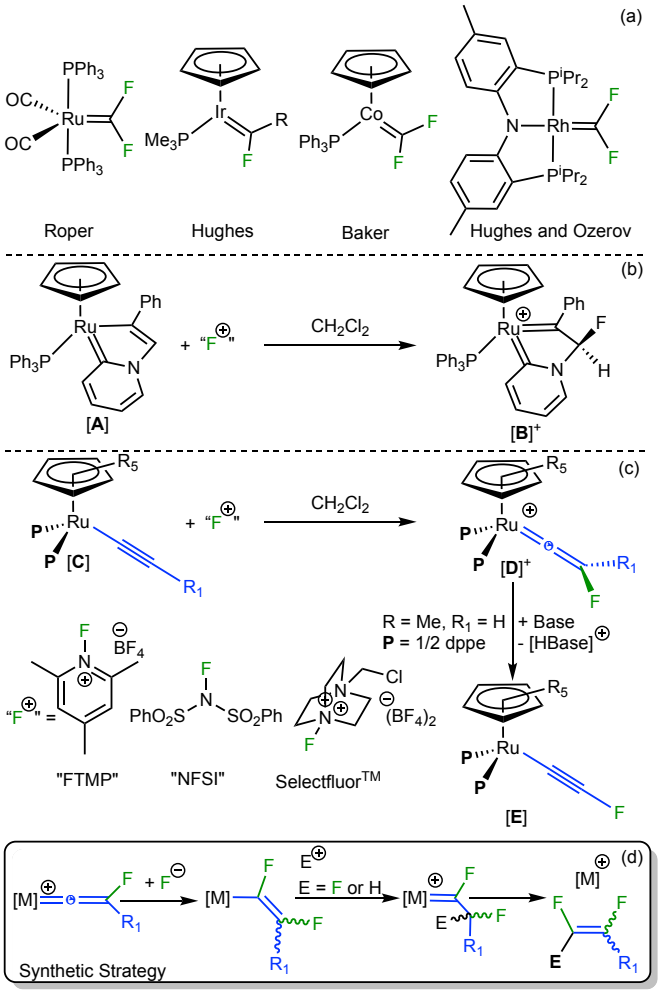
The construction of fluorocarbene ligands within the coordination sphere of transition metal complexes using sequential nucleophilic and electrophilic addition to a vinylidene complex is described. Reaction of [Ru(η^5-C_5H_5)(dppe)(=C=CPhF)][$N(SO_2Ph)_2$] with [NMe_4]F results in nucleophilic attack fluoride at the metal-bound carbon of the vinylidene ligand to give alkenyl complex [Ru(η^5-C_5H_5)(dppe)(-CF=CFPh)]. Subsequent eletrophilic fluorination with *N*-fluorobenzenesulfonimide (NFSI) results in the formation of the fluorinated carbene complex Ru(η^5-C_5H_5)(dppe)(=CF-CHFPh)][$N(SO_2Ph)_2$]. The fluorocarbene complexes undergo rearrangement to liberate free fluorinated alkenes, a process governed by the choice of solvent and anion, representing a new metal-mediated route to fluorinated alkenes from alkynes.

Introduction

Organofluorine chemistry has huge economic and societal importance in fields such as pharmaceuticals, agrochemicals, materials science and refrigerants. The introduction of fluorine into biologically active molecules can result in advantageous changes in lipophilicity and greater metabolic stability. Fluoroalkyl and fluoroaryl groups are common in medicinal and agrochemicals and,[1] in this context, fluoroalkenyl moieties are used as mimics for amide bonds.[2, 3] In addition, the use of fluoroalkenyls as refrigerants is becoming increasingly important because molecules such as 2,3,3,3-tetrafluoropropene have considerably lower global warming potentials than both chlorofluorocarbons (CFCs) and hydrofluorocarbons (HFCs). There is therefore a desire to develop efficient and selective synthetic methods to prepare organofluorine compounds, including fluoroalkenes.

Transition-metal complexes can support ligands such as carbenes, carbynes and vinylidenes, which are usually short-lived in the absence of the metal. Access to these species has enabled the discovery of many important catalytic reactions including alkene and alkyne metathesis as well as C-H functionalisation.[4]

Therefore, the synthesis of complexes bearing *fluorinated* carbene, carbyne and vinylidene ligands has significant potential to underpin the development of novel synthetic processes in organofluorine chemistry.[5] However, the synthesis of metal complexes containing these ligands can be difficult and unselective.[6] For example, the synthetic routes to the majority of



Scheme 1 (a) Previously reported fluorinated carbene complexes (b) OSEF reaction of a pyridylidene complex (c) synthesis of a fluorinated alkynyl ligand using OSEF (d) synthetic strategy used in this work.

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fluorocarbene complexes prepared to date (Scheme 1a) involve the addition or activation of a (per)fluorinated organic compound to an organometallic species to give a fluoroalkyl complex, which forms the carbene on reduction[7-10] or though spontaneous fluoride elimination.[11-13] Although these routes have proved to be insightful, the lack of a general approach has entailed that there are far fewer fluoro-substituted compounds compared to the vast number of related Fischer carbene complexes with methoxy or amino groups.

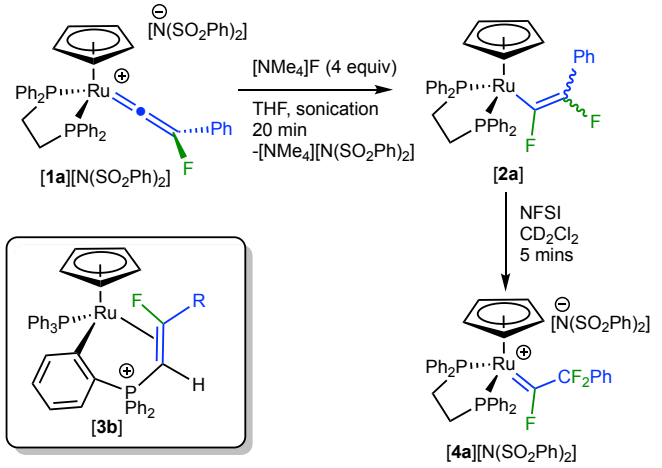
An alternative and potentially powerful approach is to use a "bottom-up" approach, which exploits the more established activation of hydrocarbon substrates and then employs the resulting species as templates to assemble the fluorinated ligands. This could be achieved by forming C-F bonds within the coordination sphere of a metal complex with either a nucleophilic (F^-) or electrophilic (formally "F^+") reagent. In a number of recent studies, we have demonstrated that outer-sphere electrophilic fluorination (OSEF) may be used to form fluorine-substituted carbenes [**B**]$^+$ (Scheme 1b),[14] vinylidenes,[15] [**D**]$^+$ and alkynyl ligands [**E**] (Scheme 1c),[16] all of which employ widely available terminal alkynes as precursors. It was envisaged that the OSEF protocol could be exploited to assemble polyfluorinated ligands within the coordination sphere of the metal. For example, the well-established electrophilicity of the metal-bound carbon atom in vinylidene ligands[17] may permit the formation of C-F bonds through addition of fluoride. This reaction would then result in the generation of a difluoroalkenyl ligand which may in turn be subjected to an OSEF reaction to give a fluorocarbene complex (Figure 1d).

Results and Discussion

Sonication of a THF solution of [Ru(η^5-C_5H_5)(dppe)(=C=CPhF)][N(SO_2Ph)$_2$], [**1a**][N(SO_2Ph)$_2$] and four equivalents of [NMe_4]F resulted in the formation of a 1:1 mixture of *E*- and *Z*-isomers of fluoroalkenyl complex [**2a**] (Scheme 2). The *Z*-isomer was characterised on the basis of characteristic resonances in the ^{19}F (δ -83.0, dt, $^3J_{FF}$ = 113 Hz $^3J_{PF}$ 28 Hz; δ -107.3, dt, $^3J_{FF}$ = 113 Hz, $^4J_{PF}$ = 3Hz) and ^{31}P (δ 92.8, dd $^3J_{PF}$ = 28 Hz, $^4J_{PF}$ = 3 Hz) NMR spectra. Resonances in the -C{^{1}H} at δ 188.2 (ddt $^1J_{CF}$ = 294 Hz, $^3J_{CF}$ = 89 Hz, $^2J_{CP}$ = 19 Hz) and δ 158.8 (dd $^1J_{CF}$ = 198 Hz, $^3J_{CF}$ = 51 Hz) were assigned to the α- and β-carbon atoms of the alkenyl ligand respectively. The *E*-isomer exhibited a similar spectroscopic features but with a smaller $^3J_{FF}$ coupling constant (10 Hz) as expected for two mutually *cis* fluorine atoms.[18]

Metal complexes containing fluorinated alkenyl ligands may be prepared from fluoroalkenes by oxidative addition and transmetallation,[19] or through C-H and C-F activation strategies.[20] However, the only other strategy for preparing these ligands from non-fluorinated organic precursors involves the electrophilic fluorination of a coordinated alkyne.[21, 22]

By using TREAT.HF ($Et_3N.3HF$) as the F^- source it was possible to control the stereochemistry of this reaction, resulting in the selective formation of *Z*-[**2a**] from [**1a**][N(SO_2Ph)$_2$], in d_8-THF solution. Treatment of the PPh_3-containing complex [Ru(η^5-C_5H_5)(PPh_3)$_2$(=C=CPhF)][N(SO_2Ph)$_2$] [**1b**][N(SO_2Ph)$_2$] with TREAT.HF resulted in the formation of both *Z*-[**2b**] and previously described [**3b**] (Scheme 2),[15] which arises from C-H bond activation of a PPh_3 ligand. To avoid this side-reaction, dppe-substituted complexes were used in subsequent studies. In addition, [NMe_4]F was used as the fluoride source since [**2a**] could be isolated more readily in these cases: the resulting chemistry was unaffected by using a mixture of *E*- and *Z*-isomers of [**2a**].



Scheme 2 Synthesis of complexes with fluorinated alkenyl, [**2a**], and carbene, [**4a**]$^+$, ligands through successive nucleophilic and electrophilic fluorination.

By analogy to the reaction in Scheme 1b, it was anticipated that addition of "F^+" to [**2a**] would give a fluorine-substituted carbene complex *via* OSEF. Addition of NFSI to a CH_2Cl_2 solution of [**2a**] resulted in a colour change from yellow to green and formation of complex [**4a**][N(SO_2Ph)$_2$] (Scheme 2). The presence of the carbene ligand was confirmed by NMR spectroscopy, which showed a low-field resonance in the ^{19}F NMR spectrum for the CF group at δ 113.6 (tt, 1F, $^3J_{FP}$ = 33 Hz, $^3J_{FF}$ = 12 Hz) as well as a related resonance for the CF_2 group at δ -90.3 (d, 2F, $^3J_{FF}$= 11 Hz). A characteristic carbene resonance at δ 284.6 (d, $^1J_{CF}$ = 399 Hz) was observed in the ^{13}C{^{1}H} NMR spectrum.

The single-crystal X-ray structure of [**4a**]PF_6 (obtained by salt metathesis from [**4a**][N(SO_2Ph)$_2$]) (Figure 1a) confirmed the presence of the fluorocarbene ligand. The Ru=C bond length, 1.872(2) Å is significantly shorter than those in related Fischer carbene complexes (*e.g.* the Ru=C bond length in [Ru(η^5-C_5H_5)(dppe)(=C{OMe}CH_2CO_2Me)][PF_6] is 1.933(4) Å).[23] When compared to fluorine, the methoxy group is a better π-donor to the carbene carbon due to closer orbital size matching and lower electronegativity. As a consequence, the methoxycarbene complexes show less π-backdonation from the metal and hence a longer M=C bond. A similar effect is observed in complexes such as [Ir(η^5-C_5Me_5)(PMe_3)(=CFCF_2CF_3)], which has a Ir=C bond length of 1.864(6) Å.[10]

Given the successful electrophilic fluorination of [**2a**], its reaction with alternative electrophiles was explored in order to provide access to hydrofluorocarbene complexes. Treatment of [**2a**] with HCl.Et_2O in CD_2Cl_2 solution resulted in the formation of [**5a**]Cl (Scheme 3). NMR spectroscopy clearly showed the presence of a hydrofluorocarbene ligand with resonances in the ^{19}F NMR spectrum for the CF group at δ 115.9 (dddd, 1F, $^3J_{FF}$ =

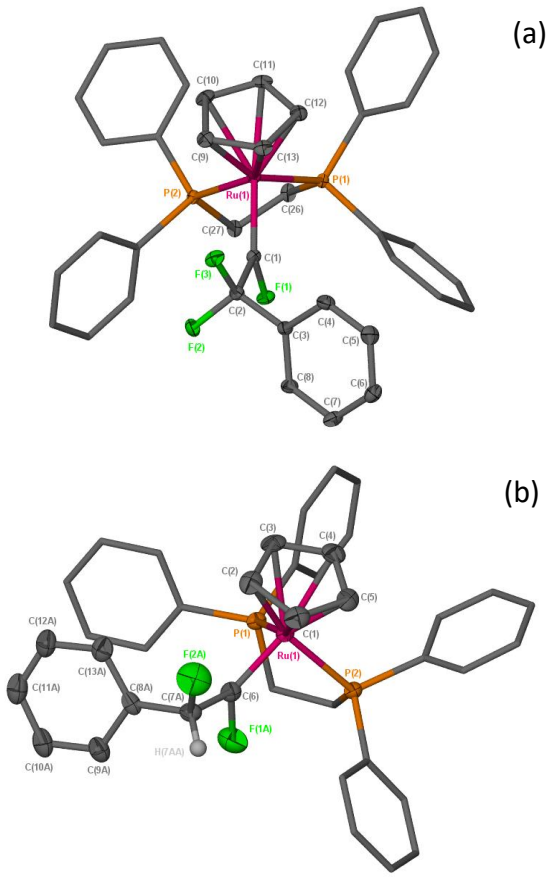
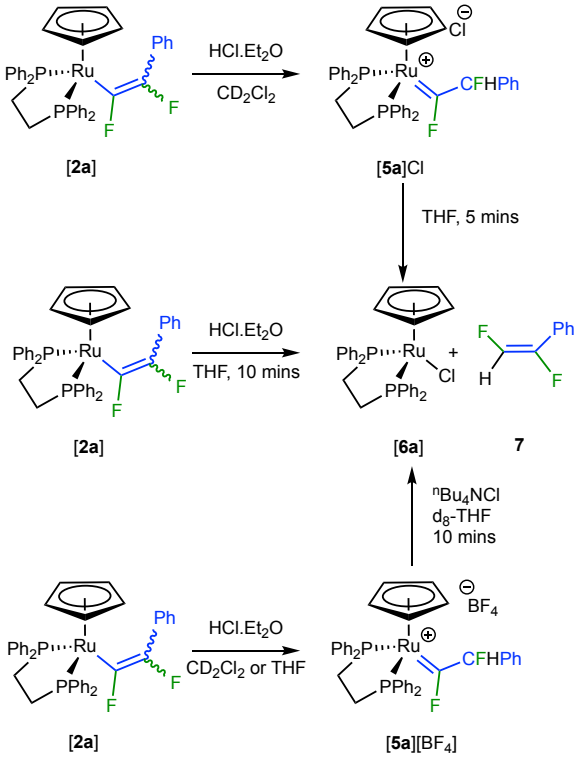


Figure 1 Structures of the cations (a) [**4a**]$^+$ and (b) [**5a**]$^+$ determined by single crystal X-ray diffraction. Thermal ellipsoids (where shown) at the 50 % probability level. Hydrogen atoms, except for H(7AA), omitted for clarity. Ruthenium shown in pink, phosphorus orange, fluorine green, carbon grey. Selected bond lengths (Å) and angles (°) for [**4a**]$^+$ Ru(1)-C(1), 1.872(2); C(1)-C(2), 1.540(3); C(1)-F(1A), 1.370(3); C(2)-F(2), 1.373(2); C(2)-F(3), 1.367(2); Ru(1)-C(1)-C(2), 132.25(26); Ru(1)-C(1)-F(1), 125.40(15); C(1)-C(2)-F(2), 107.02(17); C(1)-C(2)-F(3), 109.99(17); C(2)-C(1)-F(2), 102.21(17); F(2)-C(2)-F(3), 105.40(17); [**5a**]$^+$ Ru(1)-C(6), 1.8416(3); C(6)-C(7A), 1.371(13); C(6)-F(1A), 1.462(10); C(7A)-F(2A), 1.47(2); Ru(1)-C(6)-C(7A), 137.4(6); Ru(1)-C(6)-F(1A), 121.2(4); C(6)-C(7A)-F(2A), 109.5(11); C(7A)-C(6)-F(1A), 100.0(7).

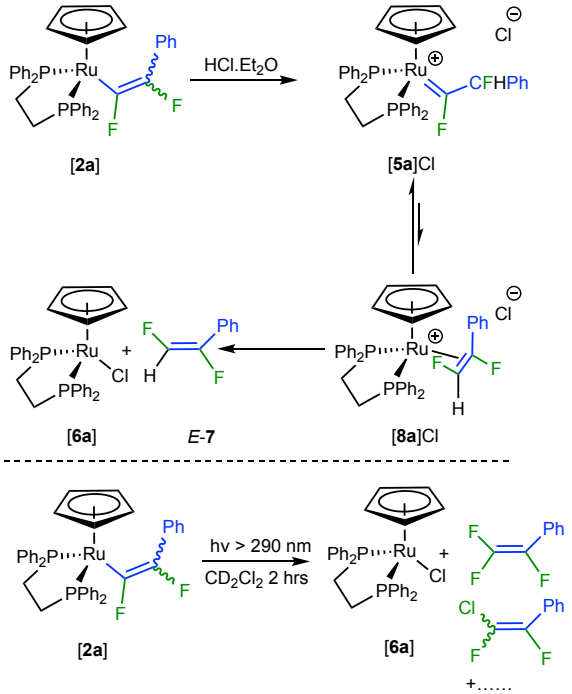
46, $^3J_{PF}$ = 43, $^3J_{PF}$ = 27, $^3J_{HF}$ = 8 Hz); and the CHF group at δ -162.9 (apparent t, $^2J_{HF}$ = 46, $^3J_{FF}$ = 46 Hz). The $^{31}P\{^1H\}$ NMR spectrum exhibited two resonances at δ 84.6 and 89.5 with a mutual 19 Hz coupling, as the creation of a stereogenic centre on the β-carbon of the carbene ligand breaks the mirror symmetry of the molecule. The structure of cation[24] [**5a**]$^+$ was also confirmed by single-crystal X-ray diffraction (Figure 1b). In a similar fashion to [**4a**]$^+$, the Ru=C bond length is much shorter (1.8416(3) Å) than in related methoxycarbene complexes.

The reaction of [**2a**] with HCl.Et$_2$O showed a remarkable solvent dependence. Performing the reaction under identical conditions, but substituting CD_2Cl_2 for THF did not afford [**5a**]Cl. Instead, rapid formation of [RuCl(η^5-C$_5$H$_5$)(dppe)] [**6a**] occurred with concomitant generation of the fluorinated alkene *E*-**7** which was identified on the basis of characteristic resonances in the ^{19}F NMR spectrum at δ -170.5 (dd, $^3J_{FF}$ = 125 Hz, $^3J_{HF}$ = 6 Hz) and δ -177.6 (dd, $^3J_{FF}$ = 125 Hz, $^2J_{HF}$ = 75 Hz).

The stereochemical outcome of this reaction gave some insight into the potential mechanism of formation of **7**. A 1:1 ratio of *E*- and *Z*-isomers of [**2a**] was used, as [Me$_4$N]F was the

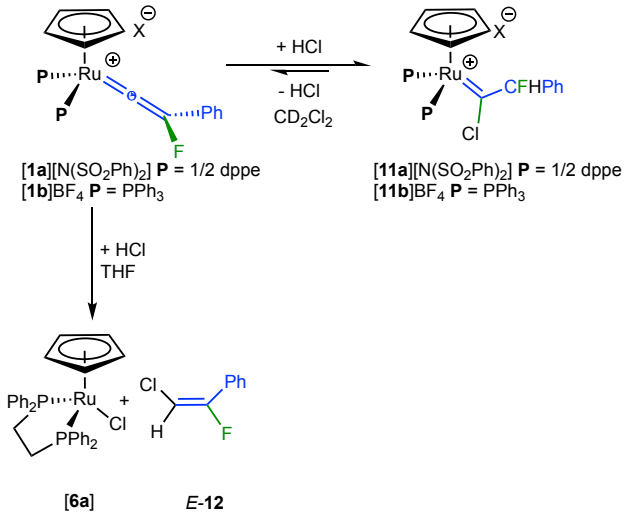


Scheme 3 Reaction of complex [**2a**] with HCl.Et$_2$O to give [**6a**] and **7** (top). Photolysis of [**2a**] in CD_2Cl_2 solution (bottom).



Scheme 4 Reaction of complex [**2a**] with HCl.Et$_2$O to give [**6a**] and **7** (top). Photolysis of [**2a**] in CD_2Cl_2 solution (bottom).

F$^-$ source for [**2a**] synthesis. Thus, the observation of only *E*-**7**, on protonation implied that the mechanism does not involve simple M-C bond protonolysis and that carbene [**5a**]$^+$ was a likely intermediate. Indeed, dissolution of [**5a**]Cl in THF resulted in immediate conversion to [**6a**] and *E*-**7** (Scheme 3). In order to



Scheme 5 Reaction of complex [**1a**][$N(SO_2Ph)_2$] and [**1b**]BF_4 with HCl.Et_2O in CD_2Cl_2 to give [**11a**]$^+$ and [**11b**]$^+$ respectively and in THF to give [**6a**] and *E*-**12**.

probe the effect of the anion on this process, [**5a**]BF_4 was prepared by reaction of [**2a**] with HBF_4.OEt_2 in CD_2Cl_2 solution (Scheme 3). In contrast to the chloride salt, dissolution of [**5a**]BF_4 in THF solution did not result in any reaction. However, addition of [^{n}Bu$_4$N]Cl to a d^8-THF solution of [**5a**]BF_4 resulted in rapid (<10 mins) formation of [**6a**] and *E*-**7**.

These data support a mechanistic picture (Scheme 4) in which [**5a**]$^+$ is formed by kinetically controlled protonation at the β-carbon of the alkenyl ligand of [**2a**]. The formation of [**6a**] and *E*-**7**, which are presumably the thermodynamic products from the reaction, involves formal proton migration in [**5a**]$^+$. The solvent and anion dependence of this process may be rationalised on the basis of an intermolecular deprotonation/protonation pathway for proton migration, in which the solvent-dependent pK_a of HCl shifts the position of equilibrium between [**5a**]$^+$ and a putative intermediate [**8a**]$^+$ (Scheme 4a), prior to displacement of the alkene. The chloride anion may be required to displace the alkene in [**8a**]$^+$ and provide a thermodynamic driving force for the reaction through formation of the stable complex [**6a**].

Further evidence for the key role of proton migration in the formation of *E*-**7** comes from the behaviour of the CF_2Ph-substituted carbene complex [**4a**][$N(SO_2Ph)_2$]. Dissolution of this complex in THF, with or without [^{n}Bu$_4$N]Cl, resulted in no fluoroalkene, F_2C=C(F)Ph, formation, indicating that neither fluorine nor phenyl migration occur under these conditions.

Fluoroalkenes may be displaced from [**2a**] by irradiation of a CD_2Cl_2 solution of the complex (λ > 290 nm) for two hours. Under these conditions, the formation of [**6a**], F_2C=C(F)Ph (**9**) and the chlorofluoroalkenes *E*- and *Z*-Cl(F)C=C(F)Ph (**10**) was observed. However, this reaction was unselective, and a number of other unidentified products were also detected. The chlorofluoroalkene **10** presumably forms *via* the photochemical generation of chlorine radicals which then react with [**2a**].

A rational synthesis of mixed Cl/F-substituted alkenes is also possible. Reaction of [**1a**][$N(SO_2Ph)_2$] or [**1b**]BF_4 with HCl in CD_2Cl_2 solution gave chlorine-substituted carbene complexes [**11a**][$N(SO_2Ph)_2$] and [**11b**]BF_4 respectively (Scheme 5). This reaction is readily reversible: elimination of HCl occurs on exposure of the compounds to vacuum. In THF solution (or with THF added to a CD_2Cl_2 solution), the reaction of [**1a**][$N(SO_2Ph)_2$] with HCl results in formation of the free *E*-H(Cl)C=C(F)Ph (**12**) and [**6a**] demonstrating that it was possible to access tetra-substituted alkenes through this method.

Conclusions

In conclusion, stepwise addition of nucleophiles and electrophiles to ruthenium fluorovinylidene complexes results in the rapid and selective formation of novel fluoroalkenyl and fluorocarbene complexes. Fluorocarbene ligand rearrangement to liberate free fluoroalkenes can be promoted by appropriate solvent and anion selection through a proton-migration pathway. Th new metal-ligand reactivity that allows for unusual fluorinated ligand systems to be constructed in a rational and controlled way from non-fluorinated substrates.

Conflicts of interest

There are no conflicts to declare.

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24. The crystal obtained was a mixture of [**1a**]$^+$ and [**5a**]$^+$ cations as well as $[PF_6]^-$ and $[SiF_5]^-$ anions.